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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/587,776	06/18/2007	Masato Miyake	690121.408USPC	2445

500 7590 04/13/2009

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EXAMINER	
GODDARD, LAURA B	

ART UNIT	PAPER NUMBER
1642	

MAIL DATE	DELIVERY MODE
04/13/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/587,776	MIYAKE ET AL.	
	Examiner	Art Unit	
	LAURA B. GODDARD	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 January 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-54* is/are pending in the application.

4a) Of the above claim(s) *3,5,9 and 24-54* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4,6-8 and 10-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *18 June 2007* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *4/9/08, 2/27/09*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. The response filed on January 29, 2009 to the restriction requirement of January 5, 2009 has been received. Applicant has elected Group I, claims 1-23, and the species of integrin receptor and CD29 for examination. Because Applicant did not distinctly and specifically point out any errors in the restriction requirement, the election has been treated as an election without traverse (MPEP 818.03(a)).

Claims 1-54 are pending. Claims 24-54 are withdrawn from further consideration by the examiner under 35 CFR 1.142(b) as being drawn to non-elected inventions. Claims 3, 5, and 9 are withdrawn as being drawn to a non-elected species. Claims 1, 2, 4, 6-8, and 10-23 are being examined as drawn to the elected species of integrin receptor and CD29.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 6-8 and 17 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 6-8 recite the limitation "the interaction molecule" and claims 6-8 depend from claim 2, however, there is no interaction molecule recited in claim 2. There is insufficient antecedent basis for this limitation in the claim.

Claim 17 recites the limitation "the cellular adhesion molecule" and claim 17 depends from claim 1, however, there is no cellular adhesion molecule recited in claim 1. There is insufficient antecedent basis for this limitation in the claim.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 1, 2, 4, 6-8, and 10-23 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a WRITTEN DESCRIPTION rejection.

The claims are drawn to **a cellular adhesion related agent** comprising an **interaction substance interacting with a cellular adhesion molecule,** wherein the interaction molecule is an antibody or derivative thereof**,** wherein the composition further comprises **a gene introduction reagent.**

The specification discloses that “cellular adhesion related agent” refers to an agent suppressing the adhesion of a cell to another substance such as a support, other cells or the like. Such an agent includes, but is not limited to interaction substances which interact with a cellular adhesion molecule. The adhesion suppression activity of such interaction substances may be confirmed by the co-existence of an interaction

substance when a cell is seeded onto a surface coated with an ECM substrate such as fibronectin. Furthermore, when substrates having such interaction activity are chemically or physically immobilized onto a surface, progress of adhesion property onto the surface of the cell is confirmed. “Interaction substances” include, but are not limited to, for example, substances allosterically interacting with a competitor, a partner in an antigen-antibody reaction (an antibody when the partner is an antigen, and an antigen when the partner is an antibody), a partner in a receptor-ligand relationship (a ligand when the partner is a receptor, and a receptor when the partner is a ligand), and the like. In the present invention, as long as cellular adhesion is enhanced, the object of the present invention (introduction of a target substance) may be achieved and thus it is to be understood that such agents are not particularly limited to a specific embodiment ([0063]). The “cellular adhesion related agent” used in the present invention comprises an interaction substance interacting with a cellular adhesion molecule such as an extracellular matrix molecule, integrin receptor, RGD molecules and the like ([0206]). In a preferable embodiment, the “interaction substance” used in the present invention causes an antigen-antibody reaction with a partner of a cellular adhesion molecule. Accordingly, the interaction substances of the present invention may be an antibody (for example, monoclonal antibodies, polyclonal antibodies, and the like), or derivatives thereof (chimeric antibodies, antibody fragments and the like) ([0207]). Preferably, the interaction substance comprises an antibody against an anti-integrin molecule, including CD49a-f relating to CD49 ([0208]). An antibody against an anti-integrin molecule, including CD29, may also be included in the preferable embodiments of the present

invention ([0210]). The term "gene introduction reagent" refers to a reagent which is used in a gene introduction method so as to enhance introduction efficiency. Examples of such a gene introduction reagent include, but are not limited to, cationic polymers, cationic lipids, polyamine-based reagents, polyimine-based reagents, calcium phosphate, and the like ([0147]). The specification does not disclose any other cellular adhesion related agents, interaction substances that interact with a cellular adhesion molecule, or gene introduction reagents as broadly encompassed in the claims.

The art (see Scott et al, J of gene Medicine, 2001, 3:125-134) teaches integrin binding motif “RGD” and an integrin binding antibody, anti-CD29 antibody, that would function as an interaction substance that binds an integrin, and a cationic liposome that would act as a gene introduction reagent, however RGD, anti-CD29 antibody, and cationic liposome do not provide an adequate representative number of species to support adequate written description for the broad genus of cellular adhesion related agents, interaction substances that interact with a cellular adhesion molecule, or gene introduction reagents as encompassed by the claims.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factor present in the claim is a recitation of “cellular adhesion related agent,” “interaction substance interacting with a cellular

adhesion molecule," or "gene introduction reagents". Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus.

Although drawn to DNA arts, the findings in University of California v. Eli Lilly and Co., 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997) and Enzo Biochem, Inc. V. Gen-Probe Inc. are relevant to the instant claims. The Federal Circuit addressed the application of the written description requirement to DNA-related inventions in University of California v. Eli Lilly and Co., 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997). The court stated that " [a] written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name', of the claimed subject matter sufficient to distinguish it from other materials. " Id. At 1567, 43 USPQ2d at 1405. The court also stated that:

> a generic statement such as "vertebrate insulin cDNA" or "mammalian insulin cDNA" without more, is not an adequate written description of the genus because it does not distinguish the genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is.

Id. At 1568, 43 USPQ2d at 1406. The court concluded that "naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material." Id.

Finally, the court addressed the manner by which a genus of cDNAs might be described. "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus." Id.

The Federal Circuit has recently clarified that a DNA molecule can be adequately described without disclosing its complete structure. See Enzo Biochem, Inc. V. Gen-Probe Inc., 296 F.3d 1316, 63 USPQ2d 1609 (Fed. Cir. 2002). The Enzo court adopted the standard that "the written description requirement can be met by show[ing] that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics ....i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics." Id. At 1324, 63 USPQ2d at 1613 (emphasis omitted, bracketed material in original).

The inventions at issue in Lilly and Enzo were DNA constructs per se, the holdings of those cases are also applicable to claims such as those at issue here. Thus, the instant specification may provide an adequate written description of cellular adhesion related agents, interaction substances that interact with a cellular adhesion

molecule, or gene introduction reagents, per Lilly by structurally describing representative cellular adhesion related agents, interaction substances that interact with a cellular adhesion molecule, or gene introduction reagents or by describing "structural features common to the members of the genus, which features constitute a substantial portion of the genus." Alternatively, per Enzo, the specification can show that the claimed invention is complete "by disclosure of sufficiently detailed, relevant identifying characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics."

In this case, the specification does not directly describe cellular adhesion related agents, interaction substances that interact with a cellular adhesion molecule, or gene introduction reagents useful in the claimed invention in a manner that satisfies either the Lilly or Enzo standards. Although the specification discloses interaction substance comprises an antibody against an anti-integrin molecule, including CD49a-f relating to CD49 or an antibody that binds CD29, and gene introduction reagents include cationic polymers, cationic lipids, polyamine-based reagents, polyimine-based reagents, calcium phosphate, and the like, this does not provide a description of the broadly claimed cellular adhesion related agents, interaction substances that interact with a cellular adhesion molecule, or gene introduction reagents that would satisfy the standard set out in Enzo because the specification provides no structural features coupled to the claimed functional characteristics.

Further, the specification also fails to describe cellular adhesion related agents, interaction substances that interact with a cellular adhesion molecule, or gene introduction reagents by the test set out in Lilly because the specification describes only interaction substances comprising an antibody against an anti-integrin molecule, including CD49a-f relating to CD49 or an antibody that binds CD29, and gene introduction reagents include cationic polymers, cationic lipids, polyamine-based reagents, polyimine-based reagents, calcium phosphate, and the like. Therefore it necessarily fails to describe a representative number of such species.

Thus, the specification does not provide an adequate written description of cellular adhesion related agents, interaction substances that interact with a cellular adhesion molecule, or gene introduction reagents that is required to practice the claimed invention.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4. Claims 1, 2, 4, 6-8, 10-19, 22, and 23 are rejected under 35 U.S.C. 102(b) as being anticipated by Scott et al (J of gene Medicine, 2001, 3:125-134), as evidenced by GIBCO product insert for OPTI-MEM® (Form No. 2017, June 2001, one page) and Kamata et al (J of Biological Chemistry, 1994, 269, 26006-26010).

The claims are drawn to a composition for enhancing the introduction efficiency of a target substance into a cell, comprising a cellular adhesion related agent (claim 1), a composition for enhancing the introduction efficiency of a target substance into a cell according to claim 1 wherein the cellular adhesion related agent comprises an interaction substance interacting with a cellular adhesion molecule (claim 2), a composition according to claim 2, wherein the cellular adhesion molecule is an integrin receptor (claim 4), a composition according to claim 2, wherein the interaction molecule raises an antigen-antibody reaction with a partner of the cellular adhesion molecule (claim 6), a composition according to claim 2, wherein the interaction molecule is an antibody or a derivative thereof (claim 7), a composition according to claim 2, wherein the interaction molecule is a monoclonal or polyclonal antibody (claim 8), a composition according to claim 1, wherein the target substance comprises a genetic material (claim 10), a composition according to claim 1, wherein the target substance comprises a nucleic acid molecule (claim 11), a composition according to claim 1, wherein the target substance comprises DNA (claim 12), a composition according to claim 4, wherein the integrin receptor is CD29 (claim 13), a composition according to claim 4, wherein then integrin receptor is selected from the group consisting of CD29 (claim 14), a composition according to claim 4, wherein the integrin receptor interacts with a molecule selected from the group consisting of collagen, fibronectin, vitronectin and laminin (claim 15), a composition according to claim 1, wherein the cell comprises at least one cell selected from the group consisting of a stem cell and a differentiated cell (claim 16), a composition according to claim 1, wherein the cellular adhesion molecule is specifically

expressed in the cell (claim 17), a composition according to claim 1, wherein the target substance is a genetic material and the composition further comprises a gene introduction reagent (claim 18), a composition according to claim 18, wherein the gene introduction reagent is selected from the group consisting of a cationic macromolecule, cationic lipid and calcium phosphate (claim 19), a composition according to claim 1 further comprising a salt (claim 22), a composition according to claim 22, wherein the salt is selected from the group consisting of salts comprised in a buffer and salts comprised in media (claim 23).

Scott et al teach a composition comprising all of: a peptide comprising the integrin-binding motif "RGD", cationic liposome, anti-CD29 antibody (anti-β1 integrin polyclonal antibody) and salts comprised in OPTI-MEM® media (p. 127, col. 1 bridging to col. 2). Scott et al teach using the composition to test DNA gene delivery to differentiated cells expressing the targeted integrin (abstract; p. 126, col. 1 to 2). The cationic liposome serves as a gene introduction agent and both anti-CD29 antibody and the RGD peptide would be interaction substances that interact or bind with integrin CD29 (β1 integrin). As evidenced by the GIBCO product insert for OPTI-MEM®, this media comprises salt sodium bicarbonate (see Formulation, col. 1). As evidence by Kamata et al, CD29 integrin inherently binds to collagen. All the limitations of the claims are met.

5. Claims 1, 2, 4, 6-8, 10-17, 20, and 21 are rejected under 35 U.S.C. 102(b) as being anticipated by Felsenfeld et al (Nature, 1996, 383:438-440).

The claims are drawn to a composition for enhancing the introduction efficiency of a target substance into a cell, comprising a cellular adhesion related agent (claim 1), a composition for enhancing the introduction efficiency of a target substance into a cell according to claim 1 wherein the cellular adhesion related agent comprises an interaction substance interacting with a cellular adhesion molecule (claim 2), a composition according to claim 2, wherein the cellular adhesion molecule is an integrin receptor (claim 4), a composition according to claim 2, wherein the interaction molecule raises an antigen-antibody reaction with a partner of the cellular adhesion molecule (claim 6), a composition according to claim 2, wherein the interaction molecule is an antibody or a derivative thereof (claim 7), a composition according to claim 2, wherein the interaction molecule is a monoclonal or polyclonal antibody (claim 8), a composition according to claim 1, wherein the target substance comprises a genetic material (claim 10), a composition according to claim 1, wherein the target substance comprises a nucleic acid molecule (claim 11), a composition according to claim 1, wherein the target substance comprises DNA (claim 12), a composition according to claim 4, wherein the integrin receptor is CD29 (claim 13), a composition according to claim 4, wherein then integrin receptor is selected from the group consisting of CD29 (claim 14), a composition according to claim 4, wherein the integrin receptor interacts with a molecule selected from the group consisting of collagen, fibronectin, vitronectin and laminin (claim 15), a composition according to claim 1, wherein the cell comprises at least one cell

selected from the group consisting of a stem cell and a differentiated cell (claim 16), a composition according to claim 1, wherein the cellular adhesion molecule is specifically expressed in the cell (claim 17), a composition according to claim 1, further comprising a particle (claim 20), a composition according to claim 20, wherein the particle comprises a gold colloid (claim 21).

It is noted that the preamble recitation of "for enhancing the introduction efficiency of a target substance into a cell" is merely suggestive of an intended use and is not given weight for purposes of comparing the claims with the prior art. The claims read on the active ingredients *per se*, which are an interaction substance interacting with a cellular adhesion molecule, (see MPEP 2111.02). It is noted that claims 10-12, 16, and 17 further limit the preamble and not the products comprised in the claimed composition, hence are not given weight for purposes of comparing the claims with the prior art.

Felsenfeld et al teach a composition comprising an anti-β1 integrin antibody (anti-CD29 antibody), wherein the integrin binds fibronectin, and gold colloid particles (p. 438, col. 1; Figure 1; Figure 3; p. 440, col. 2).

6. **Conclusion:** No claim is allowed.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to LAURA B. GODDARD whose telephone number is (571)272-8788. The examiner can normally be reached on 7:00am-3:30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Laura B Goddard/
Primary Examiner, Art Unit 1642